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EXAMINER

NIEBAUER, RONALD T

ART UNIT

PAPER NUMBER

1654

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/579,921	Applicant(s) BOMSEL ET AL.	
	Examiner RONALD T. NIEBAUER	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 September 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-34, 36-38 and 40-44 is/are pending in the application.
- 4a) Of the above claim(s) 23-33 and 42-44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34, 36-38, 40-41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicants amendments and arguments filed 9/11/09 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn. It is noted that the claim amendments have overcome the 102b rejection based on Myles, the 101 rejection, and the 112 written description rejection.

Previously, Applicant's elected Group I (claims 34-41) and the species of SEQ ID NO:9 (i.e. CysSerPheGluGluCys wherein a disulfide bond connects the Cys residues) in the replies filed on 9/8/08 and 2/2/09 is acknowledged.

In the instant case, the prior art obviate the elected species. Any art that was uncovered during the search for the elected species that reads on non-elected species is also cited herein. In accord with section 803.02 of the MPEP the claims have been examined fully with respect to the elected species.

Claims 1-22,35,39 have been cancelled.

Claims 23-33,42-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/8/08 and 2/2/09.

Claims 34,36-38,40-41 are under consideration.

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Claim Rejections - 35 USC § 112

Previously claims were rejected under 112 2nd paragraph. Since the claims have been amended a new rejection based on the amendments appears below. Since this is a new rejection, applicants arguments are not applicable to the instant rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34,38,41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 34,38 and dependent claim state m is equal to 0 to 14 and n is equal to 0 to 14 and $m+n$ is less than or equal to 5. The numerical values recited in the claim are not consistent. The claims state that m is equal to 0 to 14. Thus it would seem that m is 14 is included in the claim. However, the claim states that $m+n$ is less than or equal to 5. If m is 14 then n is negative 9, for example. However, negative numbers do not seem to make sense in the context of the instant claims. The most that either m or n can be, based on $m+n$ is less than or equal to 5, is 5. Thus, the values of m and n are unclear since it is unclear what purpose values 6-14 serve for m and n . It is unclear if the intent is such that m or n can be 6 to 14 or if the intent is such that m or n can be 0 to 5. As such, there is more than one reasonable interpretation of the claims.

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Claim Rejections - 35 USC § 102

Claims were previously rejected based on Krstenansky et al (Biochimica et biophysica acta 957 (1988) 53-59). Since the claims have been amended, an updated rejection appears below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 34,38,41 are rejected under 35 U.S.C. 102(b) as being anticipated by Krstenansky et al (Biochimica et biophysica acta 957 (1988) 53-59; first cited with office action 6/11/09).

Krstenansky teach synthetic peptides cyclized via disulfide linkages (abstract). Krstenansky teach that peptides were synthesized and that monomers were separated from oligomers (connecting sentence of column 1 and 2 of page 54) and that evidence for cyclization was obtained (page 54 2nd column). Krstenansky specifically teach the cyclic peptide (cyclized via disulfide linkages) of sequence CDFEEIPEEYLC (compound 2 of Table I). Such peptide is a cyclic peptide that comprises FEE as recited in claim 34.

Although unclear (see 112 2nd rejection above) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP section 2111). Since the claims state that m is equal to 0 to 14 and n is equal to 0 to 14, the peptide of Krstenansky is interpreted as reading on instant claim 34.

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Since Krstenansky teach that peptides were synthesized and that monomers were separated from oligomers (connecting sentence of column 1 and 2 of page 54), multimers were necessarily present as recited in claims 38. Since Krstenansky teach that the peptides were used in assays (page 54 for example) the peptides were present in a composition as recited in claim 41. It is noted that claim 41 recites 'intended for gamete culture'. Such statement is an intended use which does not result in a structural difference. Thus, Krstenansky meet the claim limitations.

Response to Arguments 102 rejection Krstenansky

Since the claims have been amended, the rejection has been adapted to the instant claims. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue (page 10) that Krstenansky does not teach the claimed invention, such as wherein $m+n$ is less than or equal to 5.

Applicant's arguments filed 9/11/09 have been fully considered but they are not persuasive.

Although Applicants argue (page 10) that Krstenansky does not teach the claimed invention, such as wherein $m+n$ is less than or equal to 5, as discussed above the claims are unclear. Claims 34,38 and dependent claim state m is equal to 0 to 14 and n is equal to 0 to 14 and $m+n$ is less than or equal to 5. The numerical values recited in the claim are not consistent. The claims state that m is equal to 0 to 14. Thus it would seem that m is 14 is included in the claim. However, the claim states that $m+n$ is less than or equal to 5. If m is 14 then n is negative

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9, for example. However, negative numbers do not seem to make sense in the context of the instant claims. It is unclear if the intent is such that m can be 0 to 14 or if the intent is such that m can be 0 to 5. As such, there is more than one reasonable interpretation of the claims.

Krstenansky specifically teach the cyclic peptide (cyclized via disulfide linkages) of sequence CDFEEIPEEYLC (compound 2 of Table I) which is interpreted as reading on the instant claims as discussed above.

Claim Rejections - 35 USC § 103

Claims were previously rejected under 103 based on the references cited below. Since the claims have been amended the rejection has been updated.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34,36-38,40-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta et al (Bioorganic and Medicinal Chemistry v8(2000) pages 723-729 as cited in IDS 5/19/06) and Bronson et al (Molecular Human Production v5 (1999) pages 433-440 as cited in IDS 5/19/06) and Myles et al (PNAS v91 pages 4195-4198 1994 as cited in IDS 5/19/06).

Gupta teach that an essential step leading to fertilization is the binding of sperm to egg (abstract). Gupta teach that fertilinBeta is a protein on the surface of sperm that mediates the binding (abstract). Gupta teach that fertilinBeta contains a highly conserved motif (D/E)ECD which suggests it could be a consensus sequence (abstract). Gupta teach that a series of linear and cyclic peptides were synthesized to characterize the binding specificity (abstract, title).

Gupta does not expressly teach the elected species of the instant invention (i.e. SEQ ID NO:9 (i.e. CysSerPheGluGluCys wherein a disulfide bond connects the Cys residues)).

Gupta does show a sequence alignment for various species and teach that the binding loop for the human sequence is RPSFECDLP (Figure 1). Gupta teach that several peptides were synthesized (page 725, Figure 2) including cyclic peptides. Gupta recognize a goal of establishing the minimal number of amino acids in the putative binding loop of fertilinBeta required for adhesion to the egg and the development of better peptidomimetic inhibitors (page 726 first column). Gupta recognize that peptides containing flanking residues (in relation to (D/E)ECD) have been tested (page 726 first column). Gupta teach that cyclic peptides were synthesized because cyclization should reduce the peptides entropy and increase binding affinity

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for its receptor (page 726 2nd column). Gupta teach that they can not yet conclude how many adjacent residues are required for binding (page 727 first column).

Since Gupta teach the development of better peptidomimetic inhibitors (page 726 first column) and teach that they can not yet conclude how many adjacent residues are required for binding (page 727 first column) one would be motivated to fine tune the experiments and determine specific peptides and peptide sequences for binding.

Bronson et al also teach that fertilin is a protein important for sperm-egg fusion (abstract). Bronson teach studies to evaluate fertilinBeta role in human fertilization by studying peptides containing an FEE sequence (abstract). Bronson teach that the FEE containing peptide inhibited adhesion of spermatozoa to eggs (page 435 2nd column). Bronson teach that the tripeptide FEE has been proposed to act as an integrin recognition site (page 438 2nd column).

Myles et al also teach the binding site in fertilin required for sperm-egg fusion (title). Myles study the role of fertilin by using peptide analogues (abstract). Myles teach (page 4196 in particular Figure 1b) the cyclized peptide CSTDEC based on guinea pig fertilin beta which was cyclized by oxidation (page 4196 2nd column 1st paragraph). Myles teach that the peptide was cyclized to better mimic the native binding site (page 4196 first column last paragraph). Myles teach that the peptides were conjugated to Covaspheres for use in assays (page 4195 2nd column).

From the sequence alignment shown in Figure 1 of Gupta one can see that the CSTDEC guinea pig fertilin beta sequence (wherein the first C is introduced for cyclization) corresponds to the sequence CSFEED of the human sequence (wherein the first C is introduced for cyclization). In other words the guinea pig sequence is STDEC and the corresponding human sequence is SFEED.

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Taken together, the references recognize the use of peptides to study the binding interactions of fertilinBeta with eggs. Since Gupta teach the development of better peptidomimetic inhibitors (page 726 first column) and teach that they can not yet conclude how many adjacent residues are required for binding (page 727 first column) one would be motivated to fine tune the experiments and determine specific peptides and peptide sequences for binding. Bronson recognizes the utility of studying the human fertilinBeta and suggests that the FEE sequence is a key region. Myles recognizes the use of cyclic peptides and specifically particular regions of the guinea pig fertilinBeta.

In summary, all of the references are focused on a core sequence of fertilinBeta either from humans or guinea pig. The references, including Gupta recognize the development of better peptidomimetic inhibitors (page 726 first column) as a goal.

Gupta does show a sequence alignment (Fig 1) for various species and teach that the binding loop for the human sequence is: RPSFEECDLP

and the loop for the guinea pig sequence is: RESTDEC DLP (Figure 1).

Bronson teach the importance of the human FEE (abstract).

Myles teach the guinea pig based sequence CSTDEC (figure 1b where the C residues are linked via a disulfide).

Taken together, based on the suggestions of the references one would be motivated to make peptides corresponding to particular regions of the human fertilinBeta protein. Since Myles teach that the peptide was cyclized to better mimic the native binding site (page 4196 first column last paragraph) one would be motivated to make cyclic peptides, particularly by incorporating cysteine residues at the N and C-terminus of a 6 amino acid sequence. Since Bronson teach the

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importance of the FEE sequence and the guinea pig peptide taught by Myles includes the corresponding residues of the guinea pig peptide one would be motivated to make the following peptide: CSFEEC where the Cys residues are linked via a disulfide bond. In other words, Myles teach the guinea pig based (i.e. from RESTDECDLP) CSTDEC peptide (wherein the Cys residues are linked via a disulfide). The corresponding human based (i.e. from RPSFEECDLP) peptide is CSFEEC where the Cys residues are linked via a disulfide bond. Since Bronson teach the use of human based peptides and specifically teach the importance of including the FEE sequence one would be motivated to use human based sequences. One would have a reasonable expectation of success based on the teachings of the references.

Since the references obviate the following peptide CSFEEC where the Cys residues are linked via a disulfide bond, the limitations of claims 34,36-37 are met. It is noted that claim 38 recites 'multimer'. However, there is no structural requirement that the 'multimer' include direct linkages. For example, the art recognizes dimers which do not require direct linkages but which are held together by weak intermolecular forces. Since Myles teach that the peptides were conjugated to Covaspheres for use in assays (page 4195 2nd column) one would be motivated to conjugate the peptides (i.e. CSFEEC where the Cys residues are linked via a disulfide bond) to Covaspheres for ease of use in assays therefore meeting the multimer limitation as recited in claims 38,40. Since the peptides are taught to be tested in assays, one would be motivated to include the peptides in compositions as recited in claim 41. It is noted that claim 41 recites 'intended for gamete culture'. Such statement is an intended use which does not result in a structural difference. Thus, the references render obvious the claim limitations.

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Although unclear (see 112 2nd rejection above) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP section 2111). Since the references obviate CSFEEC where the Cys residues are linked via a disulfide bond the structural limitations of claims 34,38 are met.

Response to Arguments 103 rejection

Since the claims have been amended, the rejection has been adapted to the instant claims. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue (pages 10-11) that one would not have been motivated by the prior art.

Applicants argue that the peptides are inhibitors of fertilization.

Applicants argue that the invention exhibits surprising ability.

Applicant's arguments filed 9/11/09 have been fully considered but they are not persuasive.

Although Applicants argue (pages 10-11) that one would not have been motivated by the prior art, the references recognize the use of peptides to study the binding interactions of fertilinBeta with eggs. Since Gupta teach the development of better peptidomimetic inhibitors (page 726 first column) and teach that they can not yet conclude how many adjacent residues are required for binding (page 727 first column) one would be motivated to fine tune the experiments and determine specific peptides and peptide sequences for binding. Bronson recognizes the utility of studying the human fertilinBeta and suggests that the FEE sequence is a key region. Myles recognizes the use of cyclic peptides and specifically particular regions of the

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guinea pig fertilinBeta. In summary, all of the references are focused on a core sequence of fertilinBeta either from humans or guinea pig. The references, including Gupta recognize the development of better peptidomimetic inhibitors (page 726 first column) as a goal. Further, it is noted that section 2143.01 I of the MPEP states: “The court found motivation to combine the references to arrive at the claimed invention in the “nature of the problem to be solved” because each reference was directed “to precisely the same problem of underpinning slumping foundations.” Id. at 1276, 69 USPQ2d at 1690. The court also rejected the notion that “an express written motivation to combine must appear in prior art references....” Id. at 1276, 69 USPQ2d at 1690.” Further, section 2141.03 of the MPEP states: “A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton.” KSR International Co. v. Teleflex Inc., 550 U.S. ___, ___, 82 USPQ2d 1385, 1397 (2007). “[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle.” Id. Office personnel may also take into account “the inferences and creative steps that a person of ordinary skill in the art would employ.” Id. at ___, 82 USPQ2d at 1396.”

Although Applicants argue that the peptides are inhibitors of fertilization, it is first noted that functional properties are not recited in claims 34,36-38,40. Claim 41 merely recites that the composition is intended for gamete culture. Such intent does not specify how the composition is to be used for the gamete culture. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, applicants have provided no evidence to support the assertion. Section 2145 I of the MPEP states that attorney argument is not the kind of factual evidence that is required to rebut a prima facie case of obviousness.

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Although Applicants argue that the invention exhibits surprising ability, section 716.02(b) of the MPEP expressly states that the burden is on the applicant to establish that results are unexpected and significant. In the instant case, it is unclear what specific results are unexpected. In the instant case, it is unclear what the instant results are compared to in order to render them unexpected. As such, it is unclear what properties one would expect. Further, it is first noted that functional properties are not recited in claims 34,36-38,40. Claim 41 merely recites that the composition is intended for gamete culture. Such intent does not specify how the composition is to be used for the gamete culture.

Prior Art of Record

The prior art previously made of record and not relied upon is considered pertinent to applicant's disclosure. Evans et al (Journal of Cell Science 108(1995) pages 3267-3278 as cited in IDS 5/19/06). Evans teach cyclic peptides of fertilin specifically from mouse (abstract). Evans teach the cyclic peptide CAQDEC. Gupta et al (cited above) teach (Figure 1) the mouse and human fertilinBeta binding loops:

Mouse: RLAQDECDVT

Human: RPSFEEDLP

Thus the mouse CAQDEC peptide corresponds to human CSFEED. Any rejection using Evans would be duplicative of the rejections above.

Conclusion

Previously claims were rejected under 112 2nd paragraph. Since the claims have been amended a new rejection based on the amendments appears below. Thus applicants amendments have necessitated new rejections. Claims were previously rejected based on Krstenansky et al (Biochimica et biophysica acta 957 (1988) 53-59). Since the claims have been amended, an updated rejection appears above. Claims were previously rejected under 103 based on the references cited above. Since the claims have been amended the rejection has been updated.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654